Reactions of Vinyl Azides and β-Haloalkyl Azides with Active Methylene Compounds. Synthesis of 1-Vinyl-1,2,3-Triazoles. (1)

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A general synthetic approach to the yet unknown class of 1-vinyl-1,2,3-triazoles is the condensation of active methylene compounds with vinyl azides or their precursors, the β-haloalkyl azides, in the presence of an alkoxide. Triazole-4-carboxylic acids prepared in this manner are decarboxylated smoothly on heating above their melting point. The use of NMR spectra in the structure assignment of some of the triazoles is discussed.

Introduction.

A general synthetic method for the preparation of 1-aryl-1,2,3-triazoles and to a lesser extent of 1-alkyl-1,2,3-triazoles is the condensation of an active methylene compound of type **2** or **4** with an aryl (or alkyl) azide in
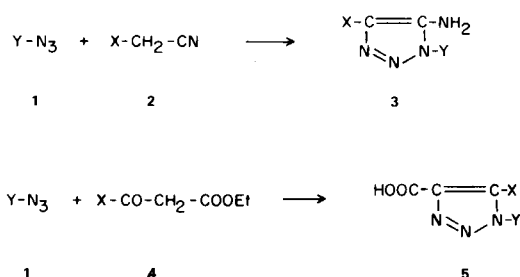
the presence of an alkoxide. The reaction was first reported by Dimroth (2) and later studied by several other investigators (3). 1-Acyl-1,2,3-triazoles (**3** or **5**, Y = R–CO–) cannot be obtained by the Dimroth method from acyl azides (**1**, Y = R–CO–) because the carbanions, generated under the reaction conditions, have a greater tendency to displace the azide group from **1** by attack at the carbonyl function, rather than to add to the terminal nitrogen of the azide (4). When sulfonyl azides (**1**, Y = R–SO₂–) are treated with active methylene compounds in the presence of bases, diazocompounds or related products are normally obtained instead of 1-sulfonyl-1,2,3-triazoles (**3** or **5**, Y = R–SO₂–) (5). The reaction of a phosphinic azide (**1**, Y = Ph₂PO–) with substituted acetonitriles, recently studied by Berlin, Ranganathan and Haberlein (6) led to phosphorylated tetrazolines instead of the expected 1-phosphorylated-1,2,3-triazoles (**3**, Y = Ph₂PO–). Since vinyl azides are available through a general method developed in our laboratory (7),

we were led to study their behaviour towards active methylene compounds.

Results and Discussion.

Condensation of vinyl azides with active methylene compounds of type **2** and **4** under the Dimroth conditions, would be expected on the basis of analogy with aryl azides (2,3) to lead to 1-vinyl-1,2,3-triazoles. This expectation was found to be correct as is illustrated in Table I. It is interesting to note that vinyl azides like aryl azides are more reactive in their condensations than are alkyl azides. All the isolated triazoles were characterized by IR and NMR and gave correct elemental analysis (see experimental section). A reasonable mechanism involves nucleophilic attack by the carbanion, derived from the active methylene compound, on the terminal nitrogen atom of the azide, followed by regiospecific (8) cyclization and aromatization to the stable triazole ring system.

β-Haloalkyl azides, when treated with active methylene compounds under the given reaction conditions, also result in 1-vinyl-1,2,3-triazoles (see Table I). The reaction can proceed either *via* the vinyl azide (*e.g.* **6 → 7 → 9**), and/or *via* direct condensation with the active methylene compound, to give a 1-(β-haloalkyl)-1,2,3-triazole (*e.g.* **8**)
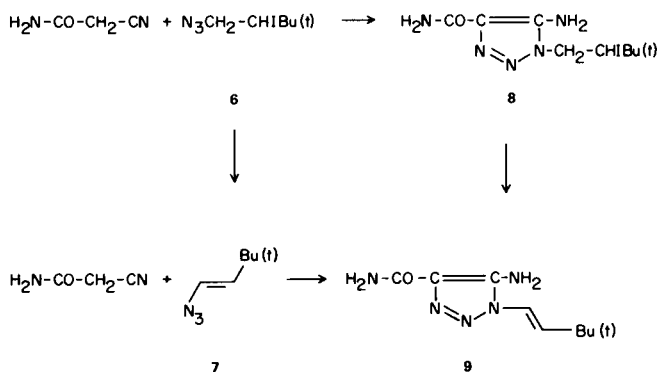
TABLE I

Synthesis of 1-Vinyl-1,2,3-triazoles (a).

$$R^4-C = C-R^5$$
$$N \diagdown N \diagup N-R^1$$

Active Methylene Compound 2 or 4	Azide	Reaction Conditions (base, solvent, temp, time)	No.	R¹	Triazole R⁴	R⁵	Yield %	M.p.
H₂N-CO-CH₂-CN	(N₃—CH=CH—Bu(t))	NaOMe, MeOH, reflux, 1/2 hour	9	CH=CH—Bu(t)	CONH₂	NH₂	62	225-226°
	N₃CH₂-CHI Bu(t)	NaOMe, MeOH, reflux, 1/2 hour					72	
	(N₃—C(=CH₂)—Ph, Bu(t))	NaOMe, MeOH, 25°, 7 days	10	(CH₂=C—Ph Bu(t))	CONH₂	NH₂	35	167-168°
	N₃CH-CH₂I Ph	NaOMe, MeOH, 25°, 7 days					44	
MeOOC-CH₂-CN	N₃CH₂-CHI Bu(t)	NaOMe, MeOH, 25°	11	CH=CH—Bu(t)	COOMe	NH₂	29	187-188°
		NaOMe, MeOH, reflux, 1/2 hour					38	
		NaOMe, MeOH, reflux, 1/2 hour					31	
PH-CH₂-CN	(N₃—CH=CH—Bu(t))	NaOMe, MeOH, 25°, 2 days	12	CH=CH—Bu(t)	Ph	NH₂	52	178-179°
		KOtBu, THF, 25°, 1 day					91	
	N₃CH₂-CHI Bu(t)	KOtBu, THF, 25°, 1 day					82.5	

Starting material	Conditions	No.	Product		R	Yield (%)	M.p.
Me-CO-CH$_2$-COOEt	NaOMe, MeOH, 25°, 5 days	13	Bu(t)	COOH	Me	67	148.5-149°
N$_3$CH$_2$-CHI Bu(t)	NaOMe, MeOH, reflux, 12 hours					84	
	NaOMe, MeOH, reflux, 24 hours					69	
Ph / N$_3$	NaOMe, MeOH, 25°, 7 days	14	Ph	COOH	Me	72	159-160°
N$_3$CH-CH$_2$I Ph	NaOMe, MeOH, reflux, 12 hours					44	
	NaOMe, MeOH, 25°, 10 days					74	
Ph / N$_3$	NaOMe, MeOH, reflux, 12 hours	15	Ph	COOH	Me	72	180° dec.
N$_3$CH$_2$-CHClPh	NaOMe, MeOH, reflux, 12 hours					55	
Ph-CO-CH$_2$-COOEt	NaOMe, MeOH, reflux, 1 day	16	Bu(t)	COOH	Ph	74	155° dec.
N$_3$CH$_2$-CHI Bu(t)	NaOMe, MeOH, reflux, 1 day					72	
Ph / N$_3$	NaOMe, MeOH, 25°, 10 days	17	Ph	COOH	Ph	69	156-157° dec.
N$_3$CH-CH$_2$I Ph	NaOMe, MeOH, 25°, 10 days					79	

(a) The superscripts in R^1, R^4, and R^5 refer to the position in the triazole ring.

followed by HI elimination to the vinyl triazole (e.g. 6 → 8 → 9). The pathway followed depends on the degree of competition between the reaction of the β-haloalkyl azide with either the alkoxide or the active methylene compound.

Decarboxylation of the 1-vinyl-5-substituted-1,2,3-triazole-4-carboxylic acids **13-17**, synthesized by reaction of ethyl acetoacetate or ethyl benzoylacetate with vinyl and β-haloalkyl azides, led to 1-vinyl-5-substituted-1,2,3-triazoles **18-22** in quantitative yield as indicated by NMR analysis of the crude reaction products.

13	R¹ = trans-t-BuCH=CH-, R⁵ = Me **18**
14	R¹ = CH₂=CPh-, R⁵ = Me **19**
15	R¹ = trans-PhCH=CH-, R⁵ = Me **20**
16	R¹ = trans-t-BuCH=CH-, R⁵ = Ph **21**
17	R¹ = CH₂=CPh-, R⁵ = Ph **22**
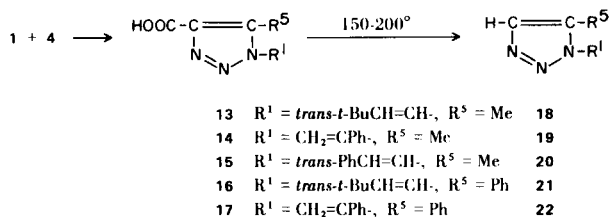
Furthermore, crude **18** analysed satisfactorily. All decarboxylated triazoles studied in this work (**18-22**) were liquids and were purified by distillation under reduced pressure. They exhibited typical triazole =C–H absorptions in the infrared spectra at about 3120 cm⁻¹.

The 5-methyl triazoles derived from the α-styryl azide or the α-azido-β-iodoethylbenzene (**14 and 19**) show in the NMR spectra a characteristic upfield shift (ca. 0.3 ppm.) for the 5-methyl absorption, compared to the other 5-methyl triazoles (**13, 15, 18, 20**). In these 1-(α-phenylvinyl)triazoles, unlike in the other vinyltriazoles, the contribution by conformation (b) affords shielding of the

(a)   (b)
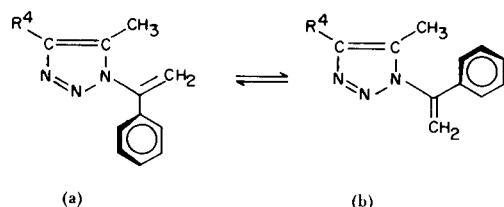
5-methyl group by the aromatic ring current in the phenyl group. The importance of this shielding effect for the eludication of regiochemistry when vinyl azides are reacted with asymmetric acetylenic compounds, has recently been described (9).

EXPERIMENTAL (10)

The β-haloalkyl azides and vinyl azides used in this work were prepared by the procedures developed in this laboratory (7).

General Procedure for the Condensation Reactions in Alcohol.

Vinyl azide or β-haloalkyl azide (0.02 mole) is allowed to react with 0.02 mole of active methylene compound in 10-20 ml. of alcohol containing 0.02 mole of alkoxide (0.04 mole of alkoxide in the case of β haloalkyl azides) under the conditions given in Table I. The reactions leading to 5-aminotriazoles (**9-12**) are worked up by addition of water and filtration of the precipitate. The reactions leading to triazole-4-carboxylic acids (**13-17**), after complete reaction, are heated for an additional hour with aqueous sodium hydroxide in order to achieve complete saponification of the ester function. The reaction mixture is then poured into hot water, acidified with hydrochloric acid, and the precipitate is filtered, washed with water and dried.

Procedure for the Condensations in Tetrahydrofuran (THF).

The azide (0.01 mole) and 0.01 mole of benzyl cyanide are added successively and dropwise to a 100 ml. of THF solution containing 0.01 mole of potassium t-butoxide (0.02 mole in the case of β-haloalkyl azides) at 0°. The whole mixture is left to stand at room temperature for 1 day and then poured into ice water, filtered and the precipitate is washed with water and dried.

Decarboxylation Experiments.

The triazole-4-carboxylic acids are heated without solvent in the temperature range of 150-200° until gas evolution ceases. Analytical samples were obtained by vacuum distillation (at ca. 150°/0.2 mm.).

1-(β-trans-t-Butylethenyl)-4-carboxamido-5-amino-1,2,3-triazole (9).

This compound was recrystallized from methanol; ir (potassium bromide), 3420 (doublet), 3270, 3140, 1640, 1625, 960 cm⁻¹; NMR (DMSO-d₆) 2.70 τ (br, 2), 3.40 (br, 2), 3.00 (d, 1, J = 14 Hz), 3.57 (d, 1, J = 14 Hz), 8.83 (s, 9).

Anal. Calcd. for C₉H₁₅N₅O (209): C, 51.68; H, 7.18; N, 33.49; O, 7.65. Found: C, 51.84; H, 7.08; N, 33.46; O, 7.78.

1-(α-Styryl)-4-carboxamido-5-amino-1,2,3-triazole (10).

This compound is hardly soluble in any common recrystallization solvent. The crude product (after washing with ethanol) however, analysed satisfactorily; ir (potassium bromide), 3450, 3400, 3350, 3270, 3160, 1645, 1620, 935 cm⁻¹; NMR (acetone-d₆) 2.55-2.70 τ (m, 5), 3.87 (d, 1, J = 1 Hz) and 4.35 (d, 1, J = 1 Hz).

Anal. Calcd. for C₁₁H₁₁N₅O (229): C, 57.64; H, 4.80. Found: C, 57.39; H, 4.94.

1-(βtrans-t-Butylethenyl)-4-carbomethoxy-5-amino-1,2,3-triazole (11).

This compound was formed in an exothermic reaction and recrystallized from methanol; ir (potassium bromide), 3450, 3280, 3220, 3160, 3120, 1685, 1625, 1245, 1120, 950 cm⁻¹; NMR (DMSO-d₆) 3.18 τ (br, s, 2, NH₂), 3.00 (d, 1, J = 14 Hz), 3.57 (d, 1, J = 14 Hz), 6.20 (s, 3), 8.85 (s, 9).

Anal. Calcd. for C₁₀H₁₆N₄O₂ (224): C, 53.57; H, 7.14; N, 25.00. Found: C, 53.38; H, 7.01; N, 24.97.

1-(β-trans-t-Butylethenyl)-4-phenyl-5-amino-1,2,3-triazole (12).

This compound was obtained from ethyl acetate-petroleum ether; ir (potassium bromide), 3320, 3210, 1640, 960 cm⁻¹; NMR (deuteriochloroform), 2.3-2.8 τ (m, 5), 3.25 (d, 1, J = 14.5 Hz) and 3.57 (d, 1, J = 14.5 Hz), 5.92 (br, 2, NH₂), 8.83 (s, 9).

Anal. Calcd. for C₁₄H₁₈N₄ (242): C, 69.42; H, 7.44; N, 23.14. Found: C, 69.67; H, 7.33; N, 23.07.

1-(β-trans-t-Butylethenyl)-5-methyl-1,2,3-triazole-4-carboxylic Acid (13).

This compound was recrystallized from benzene and contained 1/3 mole benzene (shown by NMR) when dried at room temperature. The benzene was easily removed by drying at 80° to furnish an amorphous triazole; ir (potassium bromide), 3300-2500 (COOH), 1680, 960 cm⁻¹; NMR (deuteriochloroform), -2.02 τ(s 1, OH), 3.28 (s, 2), 7.33 (s, 3), 8.80 (s, 9).

Anal. Calcd. for C₁₀H₁₅N₃O₂ (209): C, 57.42; H, 7.18; N, 20.09; O, 15.31. Found: C, 57.20; H, 7.25; N, 20.04; O, 15.63.

1-(α-Styryl)-5-methyl-1,2,3-triazole-4-carboxylic Acid (14).

This compound was obtained from chloroform-carbon tetrachloride; ir (potassium bromide), 3200-2400, 1680, 930 cm⁻¹; NMR (deuteriochloroform), -1.44 τ (s, 1), 2.5-3.0 (m, 5), 3.93 (d, 1, J = 1.5 Hz), 4.35 (d, 1, J = 1.5 Hz), 7.60 (s, 3).

Anal. Calcd. for C₁₂H₁₁N₃O₂ (229): C, 62.88; H, 4.80; N, 18.34; O, 13.97. Found: C, 62.76; H, 4.90; N, 18.22; O, 14.08.

1-(β-trans-Phenylethenyl)-5-methyl-1,2,3-triazole-4-carboxylic Acid (15).

trans-1-Azido-2-phenylethylene was prepared from the chlorine azide adduct of styrene by treatment with potassium t-butoxide in ether. After chromatography on neutral aluminum oxide, activity 1, (elution with petroleum ether) the sample showed in the NMR the presence of the vinyl azide, contaminated with ca. 20% α-styryl chloride. The yield of 15 reported in Table I is not corrected for this impurity. Triazole 15 was recrystallized from methanol; ir (potassium bromide), 3200-2400, 1675, 950 cm⁻¹; NMR (DMSO-d₆) 1.9-2.7 τ (m, 8), 7.30 (s, 3).

Anal. Calcd. for C₁₂H₁₁N₃O₂ (229): C, 62.88; H, 4.80; N, 18.34; O, 13.97. Found: C, 62.67; H, 4.63; N, 18.26; O, 14.10.

1-(β-trans-t-Butylethenyl)-5-phenyl-1,2,3-triazole-4-carboxylic Acid (16).

This compound crystallized with 1 mole of methanol (shown by NMR). The methanol was removed by drying at 80°; ir (potassium bromide), 3200-2400, 1685, 945 cm⁻¹; NMR (deuteriochloroform), -2.16 τ (s, 1), 2.50 (s, 5), 3.21 (d, 1, J = 14.5 Hz) and 3.50 (d, 1, J = 14.5 Hz), 8.92 (s, 9).

Anal. Calcd. for C₁₅H₁₇N₃O₂ (271): C, 66.42; H, 6.27; N, 15.50; O, 11.81. Found: C, 66.36; H, 6.28; N, 15.41; O, 11.73.

1-(α-Styryl)-5-phenyl-1,2,3-triazole-4-carboxylic Acid (17).

This compound was obtained from chloroform-carbon tetrachloride; ir (potassium bromide), 3200-2300, 1685, 1630, 940 cm⁻¹; NMR (deuteriochloroform), -0.11 τ (s, 1), 2.72 (s, 5), 2.65-2.95 (m, 5), 4.15 (d, 1, J = 1.5 Hz) and 4.45 (d, 1, J = 1.5 Hz).

Anal. Calcd. for C₁₇H₁₃N₃O₂ (291): C, 70.10; H, 4.47; N, 14.43; O, 11.00. Found: C, 70.10; H, 4.58; N, 14.51; O, 11.21.

1-(β-trans-t-Butylethenyl)-5-methyl-1,2,3-triazole (18).

This compound is a colorless liquid after vacuum distillation; ir (neat) 3130, 3080, 1660, 960 cm⁻¹; NMR (deuteriochloroform), 2.57 τ (s, triazole CH), 3.21 (d, 1, J = 14.5 Hz), 3.50 (d, 1, J - 14.5 Hz), 7.67 (s, 3), 8.80 (s, 9).

Anal. Calcd. for C₉H₁₅N₃ (165): C, 65.45; H, 9.09; N, 25.45. Found (for the crude reaction product): C, 65.25; H, 9.11;

N, 25.23. Found (for the analytical sample): C, 65.62; H, 9.10; N, 25.48.

1-(α-Styryl)-5-methyl-1,2,3-triazole (19).

This compound was obtained as an orange liquid after vacuum distillation; ir (neat) 3110, 1640, 975, 915 cm⁻¹; NMR (deuteriochloroform), 2.48 τ (s, triazole CH), 2.6-3.0 (m, 5), 4.07 (d, 1, J = 1 Hz), 4.48 (d, 1, J = 1 Hz), 7.93 (s, 3).

Anal. Calcd. for C₁₁H₁₁N₃ (185): C, 71.35; H, 5.94; N, 22.70. Found: C, 71.19; H, 6.12; N, 22.86.

1-(β-trans-Phenylethenyl)-5-methyl-1,2,3-triazole (20).

This compound was a highly viscous yellow oil after vacuum distillation which solidified after a few days; ir (neat) 3130, 1650, 950 cm⁻¹; NMR (deuteriochloroform), 2.5-2.8 τ (m, 8), 7.65 (s, 3).

Anal. Calcd. for C₁₁H₁₁N₃ (185): C, 71.35; H, 5.94; N, 22.70. Found: C, 71.42; H, 5.91; N, 22.61.

1-(β-trans-t-Butylethenyl)-5-phenyl-1,2,3-triazole (21).

This compound was obtained as a pale yellow liquid after vacuum distillation; ir (neat) 3120, 1660, 970, 960 cm⁻¹; NMR (deuteriochloroform), 2.30 τ (s, triazole CH), 2.53 (s, 5), 3.17 (d, 1, J = 14 Hz), 3.43 (d, 1, J = 14 Hz), 8.87 (s, 9).

Anal. Calcd. for C₁₄H₁₇N₃ (227): C, 74.01; H, 7.49; N, 18.50. Found: C, 74.29; H, 7.55; N, 18.74.

1-(α-Styryl)-5-phenyl-1,2,3-triazole (22).

This compound was obtained as a highly viscous orange oil after vacuum distillation; ir (neat) 3120, 1640, 1015, 1005, 920 cm⁻¹; NMR (deuteriochloroform), 2.17 τ (s, triazole CH), 2.6-3.0 (m, 10), 4.14 (d, 1, J = 1 Hz), 4.50 (d, 1, J = 1 Hz).

Anal. Calcd. for C₁₆H₁₃N₃ (247): C, 77.73; H, 5.26; N, 17.01. Found: C, 77.83; H, 5.48; N, 17.08.

Acknowledgment.

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